Reactions to Chilling of the Body Surface.

Experimental Study of a Possible Mechanism for the Excitation of Infections of the Pharynx and Tonsils.*

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I. Introductory. — It is a fact abundantly established that pathogenic microörganisms may exist for long periods upon the healthy mucous membranes of healthy individuals. There is evidence also that changes in the internal or external conditions of such a healthy carrier may initiate infectious processes in the mucous surfaces in which these same microörganisms are the active agents. Of these exciting causes of pharyngitis, tonsillitis and rhinitis, among the most commonly cited is chilling of the body surfaces.

Search for a mechanism by which exposure of the external body surfaces could so influence the mucous membranes as to allow of their infection has led to various hypotheses. Wright points to a " local biochemical change " brought about reflexly through the sympathetic nervous system.[1] The idea more commonly advanced, although without experimental warrant, is that the reflex cutaneous vasoconstriction incident on chilling, driving the blood to internal organs, gives rise to congestion and stasis in the mucous-membrane vessels, thus lowering resistance to the bacterial flora present.[2, 3]

Direct experimental inquiry as to what actually does take place upon the human mucous membranes when the body surface is chilled has been singularly lacking. With the hope of making a beginning at supplying this deficiency, the present experiments were undertaken. The changes investigated have been, primarily, those in the vasomotor conditions of the membranes. The mucous membranes of the palate, faucial tonsils, oropharynx and nasopharynx have been studied.

* Received for publication May 8, 1919.

It may at once be said that the traditional idea outlined above, to the effect that congestion follows chilling, is precisely the opposite of what in reality does occur; chilling was found to be followed instead by reflex vasoconstriction and ischemia.

II. Material and methods. — The experiments from which all the tables and curves published were taken were performed upon human subjects.

Of the several criteria of vascular condition, heat seemed most readily susceptible of quantitative study. Estimation by inspection of the redness of the mucosæ was used as a check.

The only skin thermometers on the market are of such shape and such large size as to be inapplicable to the study of superficial temperature changes in the sites under consideration. Recourse was therefore had to thermogalvanometry.

Apparatus used: Two similar three-element thermopiles were made up of German silver wire, No. 30, and of copper wire, No. 25. In making each thermopile, three lengths of the German silver wire about a yard long were soldered alternately to three pieces of copper wire of the same length. The wires were then folded together to make a single bundle of six strands with three German silver-copper junctions at one end for application to the surface of unknown temperature, and two junctions and a loose end of copper and another of German silver at the other end of the bundle, which was to be kept at a known temperature. To each of the loose ends was soldered a copper wire leading to a rocking key. The known-temperature end of the thermopile was packed in cotton with a sensitive thermometer in a test tube suspended in the room by a clamp about its neck.

A second three-element thermopile was similarly arranged and connected to the rocking key. From this key copper wires were led to a D'Arsonval galvanometer. Thus, by pushing down, successively, the two ends of the rocking key, each of the thermopiles could be brought successively and separately into circuit with the galvanometer.

The unknown-temperature end of the mucous membrane thermopile, when applied, was continuously bathed in mucus, containing electrolytes. Its terminals had therefore to be insulated from each other; this was accomplished by dipping them repeatedly into an alcoholic solution of shellac. The skin thermopile was similarly protected against short circuiting by sweat. The adequacy of the insulation was proved by calibrating the thermopile both in salt solution and in distilled water.

The sensitivity of the apparatus above described was such that one millimeter deflection on the galvanometer scale indicated a temperature difference of about one-tenth degree centigrade between the two ends of the thermopile in the circuit.

For calibration, the unknown temperature terminals of the thermopile were bound with elastic about the bulb of a sensitive thermometer and this was immersed in a suspended test tube of distilled water or salt solution. The water was then very slowly heated from outside, and meanwhile stirred. The galvanometer deflection and temperature of the two ends of the thermopile were read at short intervals. From this data calibration curves for the thermopiles were constructed. Since these were found to be virtually straight lines within the temperature range of the experiments, the results were averaged for each thermopile and calibration constants thus obtained.

For the skin thermopile, 1 mm. galvanometer deflection was equivalent to .1004° C. temperature difference between the two ends. The probable error of the determination was ±.0037.

For the mucous-membrane thermopile as used in experiments 1 to 7 inclusive, 15 and 16, the calibration constant found was .1054±.00044. The mucous-membrane temperatures computed from this constant were probably a degree or more too high, a difference too large to be accounted for by the probable error of the determination. It is probable, therefore, that the calibration method involved a "systematic error." Had it been necessary, this small error might have been eliminated by using a Beckmann freezing-point apparatus or other elaborate and time-consuming means. However, we were concerned primarily with superficial temperature changes, not with absolute temperatures, and the error introduced into the determination of such changes by a slight inaccuracy in the calibration constant was so minute as to be negligible.

For the later experiments, 17 to 26 inclusive, new applying terminals were made for the mucous-membrane thermopile. The calibration constant determined in physiological salt solution was, 1 mm. = .0896° ±.00021. In distilled water, 1 mm. = .0936° ±.00013. The constant used was the average, 1 mm. = .0916° C.

Application of the thermopile terminals: The phase of the thermogalvanometric study of the skin and mucous surfaces which presented a new problem was that of applying the unknown temperature ends of the thermopiles. They had to be so fixed upon the site to be studied that they would remain in unchanged position, under constant and light pressure, and in such a way as not to interfere with the rise and fall of temperature in the surfaces under them in response to changing vasomotor conditions. The first two requirements were met by fastening the thermopile wires upon stiff carriers which we may designate as "applicators," and then fastening the latter to the appropriate surfaces by strips of adhesive plaster. Various applicators of carved wood and of wood padded with cotton covered with adhesive plaster were tried and rejected because they interfered with the normal loss of heat from the surfaces under them. Applicators satisfactory in all respects were finally made from galvanized iron wire. A medium size was used (No. 10), such that it could be twisted and hammered into the required shapes, yet would bear considerable pressure without deformation.

The several applicators used in the experiments to be considered below are shown in Fig. I. Each consists of a body along which the thermopile wires are strung and the adhesive supports placed, and a tip just large enough to allow the three terminals of the thermopile to be twisted around it. The tip is so shaped as to conform to the contour of the surface against which it is to hold the thermopile terminals. The terminals, although insulated with shellac as described above, are separated from the metal tip by a single strip of adhesive plaster as a further safeguard against short-circuiting (See Fig. I., A^1 and D).

The skin applicators (Fig. I.: A and A^1) are so shaped as to form a bridge, resting stably on a support at either end, one of which is the tip, bearing the terminals. Across this raised bridge are placed the adhesive straps which hold the device in position on the skin. The tip rested usually either in the subject's supra-clavicular fossa or on the forehead.

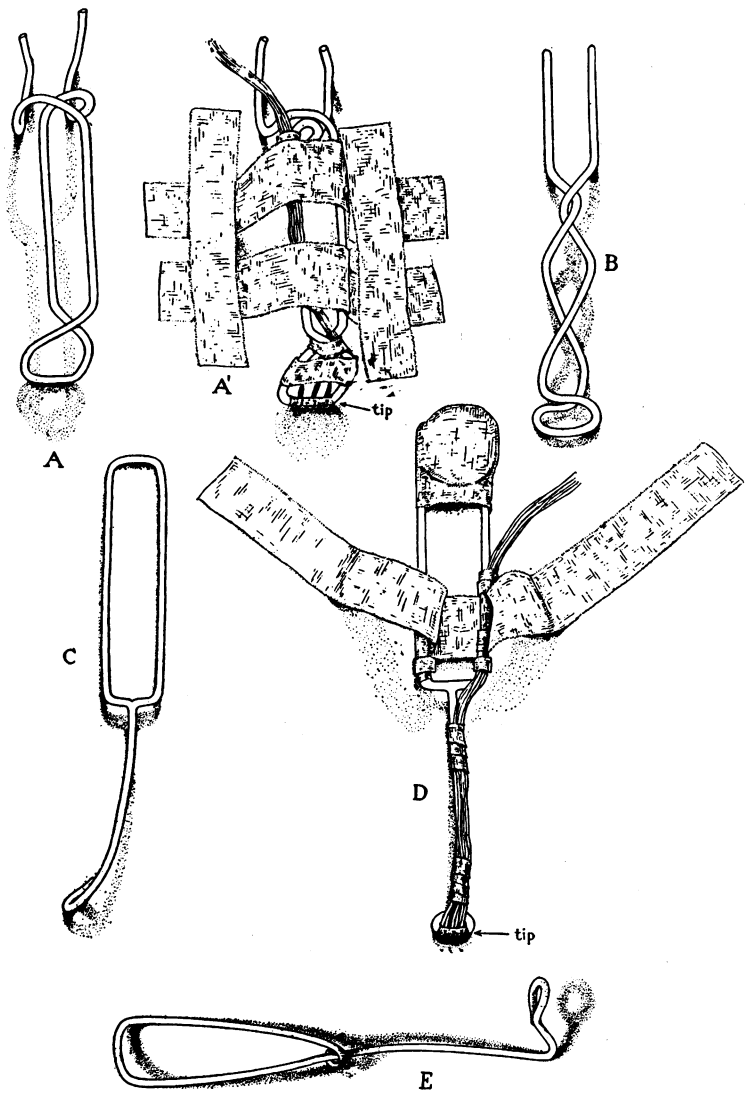

FIG. I. — Applicators: A, for skin; A^1, same, applied; B, for soft palate; C, for faucial tonsils; D, for oropharynx, ready for application; E, for nasopharynx.

The mucous-membrane applicators (Fig. I.: B, C, D and E) are in each case slung in the subject's open mouth by a long adhesive strip (Fig. I.: D), which supports the body of the applicator, then passes up just in front of the corners of the mouth and is fastened on the subject's two cheeks. The tip of the applicator holds the thermopile terminals against the particular site on the palate, tonsil or pharynx whose temperature changes are to be studied. The other end of the applicator projects out of the subject's mouth and bears a small weight. Thus the whole device when in position constitutes a lever whose fulcrum is the supporting adhesive strip, whose short arm is weighted and the tip of whose long arm holds the thermopile end against the mucous surface.

Arrangement of the subject: The experiments were performed in a constant-temperature room, kept, on the average, between eighteen and nineteen degrees centigrade. The subject entered the room undressed save for shoes and socks, but warmly wrapped in loose garments. Throughout each experiment he sat in unchanging position, mouth held wide open by a cork between his teeth, tongue held flat on the floor of his mouth, and applicator in position. The sites on which the applicators were placed were of course never wrapped and were protected from direct chilling. The experimenter removed and reapplied the wraps without disturbing the subject. Chilling was effected by (*a*) removing the wraps, or (*b*) unwrapping and applying cold wet towels to the subject's back; or (*c*) unwrapping and turning an electric fan upon the subject's back. The third method was found to be by far the most efficacious.

Factors determining superficial temperature changes: The factors determining the temperature changes in the skin and mucous surfaces during the course of an experiment may now readily be understood. The skin is a plane surface constantly being heated from below by the circulating blood in the cutaneous vessels (and to a less extent by direct conduction of heat from the deeper tissues) and constantly losing heat by radiation, conduction and convection to the cold air of the

room to which it is exposed. Since the temperature of the room (and of the deeper body tissues) remains virtually constant throughout the experiment, the skin temperature depends primarily upon two variable factors, viz., (*a*) the blood temperature and (*b*) the amount of blood per unit of time which circulates through the cutaneous vessels. Of these the latter is incomparably the more important. For although a rise or fall in blood temperature would of course tend to effect a corresponding change in skin temperature, yet such blood-temperature changes under the conditions of our experiments were found to take place only to a relatively slight degree. It is a fact of much greater moment, that, as more blood circulates through the skin, the superficial temperature must rise, that as the cutaneous arterioles are constricted the superficial temperature must fall.

For theoretical completeness, alterations in rate of evaporation of sweat must also be considered. However, with the sudden changes from warmth to chilling and vice versa used in our experiments, sweat evaporation changes must have played a small part; and whatever part it did play must have been simply to make less striking the primarily important effects of vasoconstriction and vasodilation. For example, chilling the body surface was found experimentally to cause a sharp fall in superficial temperature due to reflex cutaneous vasoconstriction. But this same chilling would decrease the production of sweat and the rate of sweat evaporation and hence tend to prevent the fall in temperature incident to vasoconstriction; and similarly for warming the body, *mutatis mutandis*.

Also in the mucous membranes the factor of prime importance in effecting temperature changes is that of vasomotor tone. Blood temperature, because of its relative constancy, is of minor interest. Room temperature, rate of evaporation of liquids and conduction of heat to the surface from deeper tissues are all virtually constant throughout the experiment, and so require no consideration. A third factor of consequence operating here must, however, be considered — namely, changes in rate and volume of respiration. We may assume the mucous membrane, warmed by the circulating blood, to be losing heat in three ways, (*a*) by direct radiation through the open mouth, (*b*) by inhalation of cool air and exhalation of

warm air in respiration, and (*c*) by conduction down a thermal gradient established through the air in the mouth, and especially along the metal applicator, to the cold room outside. From what has been said above it is evident that the rate of heat loss by (*a*) radiation, and by (*c*) conduction, was kept virtually constant throughout each experiment. In the early work, (*b*) respiration was not kept constant. In all the crucial experiments, however, respiration was carefully controlled, as will be indicated below.

The thermopiles when applied to such surfaces under the conditions described do not record precisely the absolute temperatures of the surfaces as they would be in the absence of the thermopiles. However, we believe that this method does afford an accurate and sensitive means of recording superficial temperature changes, and, through these, states of vasomotor tone, and it is with these that we are concerned.

III. Course of the experiments. — Experiments on dogs: The method was first tried out on dogs. However, the anæsthesia, necessary on technical grounds, so interfered with reflexes that few results of value were obtained. In one experiment under light anæsthesia by the closed nitrous oxide-oxygen and ether method[4] a fall of .3° C. in cranial skin temperature and of .5° C. in palatine mucous-membrane temperature followed chilling of the body surface. Upon drying and wrapping the dog, the skin temperature rose 2.0° C. and the mucous-membrane temperature about .15° C. These observations on dogs, although in accord with the accurate results with human subjects, are not above question because of imperfect technic.

In another dog experiment a transient fall of 2.0° C. in palatine mucous-membrane temperature followed intravenous injection of adrenalin (2 cc. of 1 : 10,000 sol.).

The blood temperature of these anæsthetized animals fell extremely rapidly, — on the average, .028° C. per minute. This fall was temporarily checked by intravenous injection of adrenalin.

Early thermogalvanometric experiments upon human subjects: Upon adopting ourselves as subjects, it at once became evident that chilling the body surface caused a marked depression of mucous-membrane temperature, paralleling a like

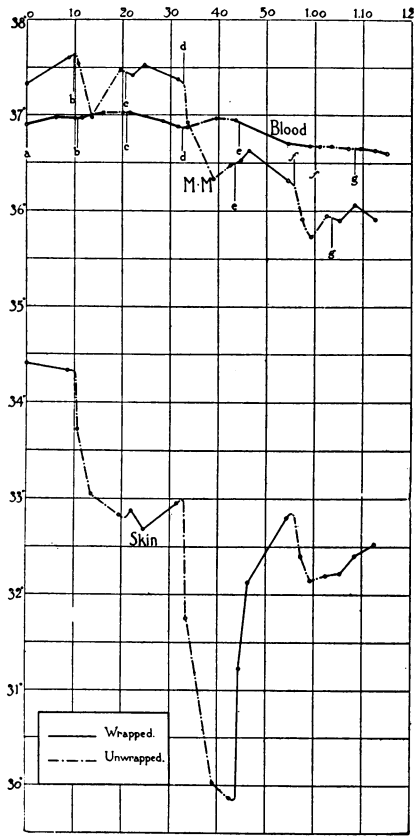

FIG. II. — Effects of Chilling Body Surface, Respiration Uncontrolled. Composite Graph, Experiments 3, 4 and 5 (Skin and Mucous-Membrane Temperatures) and Experiments 8, 9 and 10 (Blood Temperature). Temperature in degrees centigrade on ordinate; time in minutes on abscissa: *a*, wrapped; *b*, unwrapped; *c*, wrapped; *d*, unwrapped, fan on back; *e*, fan off, wrapped; *f*, unwrapped, cold wet towels to back; *g*, dried, wrapped.

fall in skin temperature. (Fig. II.) Thus, in nineteen instances of exposure to cold, a fall in mucous-membrane temperature resulted in seventeen instances, — seven in seven cases of

chilling by cold wet towels, six in six by the electric fan, and four in six chillings by mere removal of wraps.

Of the two exceptions, in Experiment 4 there was an almost steady rise in mucous-membrane temperature from a time shortly after readings were begun and lasting for some twenty-three minutes, including the period during which the subject was unwrapped; local hyperæmia resulting from mechanical irritation of the pharyngeal mucosa was the probable cause. The second exception, Experiment 6, did, as a matter of fact, give a very slight transient fall followed by return to above control level.

The average maximum mucous-membrane temperature falls were: for chilling by mere unwrapping, .51° C., developed in 8.25 minutes; for chilling with fan, .81° C. in 6.5 minutes; for chilling with cold, wet towels to back, .64° C. in 3.7 minutes.

The average skin-temperature depressions developed in the same time intervals in the same experiments were: unwrapping, 1.40° C.; chilling with fan, 2.73° C.; with cold, wet towels, .57° C.

The greater efficacy of a moving current of air as compared to mere cold applications as a means of chilling is well shown here.

Seven experiments showing these changes are briefly summarized below.

Experiment 1. — S. B. G., subject. Skin thermopile in left infraclavicular fossa. Mucous-membrane applicator at anterior border of soft palate. Room temperature, 20.3 to 21.0° C.; time, 8:55 to 10:00 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M.M. Temp.
Wrapped	0:00	32.15°	36.96°
At 0:01, unwrapped, fan on back	0:05	30.00°	36.20°
Unwrapped, fan on back	0:13.5	29.30°	36.55°
Wrapped	0:00	31.65°	34.15°
At 0:01, unwrapped, cold towels to back	0:08	31.85°	32.82°
At 0:09, dried, wrapped	0:16.5	29.95°	32.93°

Experiment 2. — S. M., subject. Skin thermopile in left infraclavicular fossa. Mucous-membrane applicator on posterior part of hard palate. Room temperature, 20.3° C. to 20.75° C.; time, 8:23 to 9:52 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M. M. Temp.
Wrapped	0:00	33.90°	35.29°
At 0:01, unwrapped	0:14.5	31.70°	33.78°
At 0:16.5, wrapped	0:29	33.65°	34.05°
Wrapped	0:00	32.55°	33.05°
At 0:01, unwrapped, fan on back	0:04	30.15°	32.30°
At 0:06.5, fan off, wrapped	0:15.5	31.30°	32.94°

Experiment 3. — S. B. G., subject. Skin thermopile in left supraclavicular fossa. Mucous-membrane thermopile on posterior part of soft palate. Room temperature, 18.25° to 18.9° C.; time, 4:28 to 5:54 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M.M. Temp.
Wrapped	0:00	35.60°	38.97°*
At 0:01, unwrapped	0:06.5	33.60°	37.54°
Unwrapped	0:12	33.13°	37.96°
At 0:13, wrapped	0:28.5	32.95°	37.96°
At 0:29.5, unwrapped, fan on back	0:41	30.10°	36.47°
At 0:45, fan off, wrapped	1:04	33.65°	36.49°
At 1:05, unwrapped, cold towels to back	1:07.5	32.55°	36.14°
At 1:12.5, dried, wrapped	1:23.5	32.65°	36.45°

*Probably too high because of inaccurate calibration constant.

Experiment 4. — S. M., subject. Skin thermopile in left supraclavicular fossa. Mucous-membrane thermopile on posterior wall of oropharynx. Room temperature, 19.3° to 20.6° C.; time 3:53 to 5:22 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M.M. Temp.
Wrapped	0:00	32.90°	35.24°
At 0:01, unwrapped	0:12.5	32.65°	36.39°
At 0:13.5, wrapped	0:19	32.00°	36.29°
Wrapped	0:26.5	32.20°	35.90°
At 0:27.5, unwrapped, fan on back	0:30.5	29.90°	35.17°
Unwrapped, fan on back	0:35.5	29.75°	35.41°
At 0:36.5, fan off, wrapped	0:45.5	32.30°	35.17°
At 0:46.5, unwrapped, cold towels to back	0:51.5	31.80°	34.33°
At 0:55.5, dried, wrapped	1:07	32.00°	34.27°

Experiment 5. — S. B. G., subject. Skin thermopile in left supraclavicular fossa. Mucous-membrane thermopile on posterior part of soft palate. Room temperature, 19.1° to 19.55° C.; time, 5:26 to 6:13 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M.M. Temp.
Wrapped	0:00	34.50°	38.59°
At 0:01, unwrapped	0:05	33.10°	37.98°
At 0:08.5, wrapped	0:13.5	33.70°	38.21°
At 0:14.5, unwrapped, fan on back	0:21	29.90°	37.37°
At 0:22, fan off, wrapped	0:25.5	32.80°	37.34°
At 0:29.5, unwrapped, iced towels on back	0:32	32.10°	36.74°
At 0:36, dried, wrapped	0:41.5	32.90°	37.02°

Experiment 6. — G. A. (Japanese), subject. Skin thermopile in left supraclavicular fossa. Mucous-membrane thermopile on middle of soft palate. Room temperature, 19.05° to 19.7° C.; time, 3:45 to 5:17 P.M.

Condition of Subject.	Time of Reading.	Skin Temp.	M.M. Temp.
Wrapped	0:00	32.95°	34.96°
At 0:00.5, unwrapped	0:03	31.80°	34.91°
Unwrapped	0:05.5	31.55°	35.00°
At 0:06, wrapped	0:12	31.60°	35.22°
At 0:12.5, unwrapped, fan on back	0:16.5	29.20°	35.03°
Unwrapped, fan on back	0:23.5	28.70°	34.92°
At 0:25.5, fan off, wrapped	0:49	31.65°	35.06°
At 0:49.5, feet in cold, wet towels; fan on feet	0:54	31.60°	34.78°
Feet in cold, wet towels; fan on feet	0:59	31.65°	34.77°
At 0:59.5, fan off, feet dried and wrapped	1:13	31.75°	34.82°
At 1:13.5, unwrapped, cold wet towels to back	1:15	31.00°	34.73°

Experiment 7. — S. M., subject. Mucous-membrane thermopile on posterior wall of oropharynx. Room temperature, 17.6° to 18.8° C.; time, 4:24 to 6:27 P.M.

Condition of Subject.	Time of Reading.	M.M. Temp.
Wrapped	0:00	36.04°
At 0:01, unwrapped	0:13.5	35.45°
At 0:14.5, wrapped	0:39	35.31°
At 0:40, cold, wet towels and fan on feet	0:51	35.54°
At 0:52, wraps off legs and thighs	0:58	34.77°
At 0:59, wraps off back; wet towels and fan on back	1:03	34.61°
At 1:07, dried, wrapped	1:18.5	34.47°

It became evident, then, that chilling of a part of the body surface regularly caused a fall also in the temperature of the mucous membranes and of areas of the skin which were protected from direct chilling. There was every reason to believe that this fall was due to reflex vasoconstriction. A considerable drop either in blood temperature or in blood pressure might, however, have produced such a depression of superficial temperature. Therefore control experiments were performed, and showed the reaction of blood temperature and pressure to chilling of the body surface to be a slight rise rather than a fall. These controls are described below.

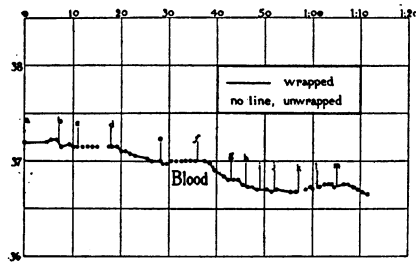

FIG. III. — Blood-Temperature Control. Experiment 10: *a*, electric light is reflected on thermometer; *b*, light removed; *c*, unwrapped; *d*, wrapped; *e*, unwrapped, fan on; *f*, fan off, wrapped; *g*, muscles of subject under tension; *h*, subject feels warm; *i*, subject sits comfortably, skin seems flushed; *j*, subject feels cold; *k*, unwrapped, cold towels to back; *l*, fresh cold wet towels to back; *m*, dried and wrapped.

Blood-temperature reactions to chilling of the body surface: The subject entered the room wrapped and was successively chilled and warmed as in the experiments cited above. Under his tongue was a sensitive thermometer; his mouth was closed. The thermometer could be read correctly to one twentieth of a degree centigrade without changing its position. The average results of three such experiments (Nos. 8, 9 and 10) were:

After unwrapping subject, a rise of .05°, developed in 5.5 minutes; subject wrapped, and there followed a fall of .14° in 11 minutes; unwrapped, fan on back, a rise of .07° in 6.8 minutes; wrapped, a fall of .275° in 14.8 minutes; unwrapped, cold towels to back, a fall of .025° in 7 minutes; wrapped, a fall of .06° in 6.8 minutes.

For a composite graph of these experiments see Fig. II.

The individual experiments are represented graphically in Figs. III., V. and IX. Experiment 8 was performed at a room temperature of 17.0° to 17.9° C.; time, 9:29 to 10:45 P.M. For Experiment 9, room temperature was 18.75° to 19.95° C.; time, 5:11 to 6:29 P. M. For Experiment 10, room temperature was 18.85° to 20.2° C.; time, 9:02 to 10:14 P.M.

Two further controls, conforming to the pattern of the later thermogalvanometric determinations to be described below, may be summarized here.

Experiment 11. — S. M., subject. Mercury thermometer under tongue. Room temperature, 18.0° to 18.8° C.; time, 7:40 to 9:49 P.M.

Condition of Subject.	Time of Reading.	Blood Temp.
Wrapped, breathing quietly	0:00	37.70°
Wrapped, breathing quietly	0:11	37.60°
At 0:12, wrapped, breathes deeply	0:15	37.55°
Wrapped, breathing deeply	0:37	37.50°
Wrapped, breathing deeply	0:44	37.51°
At 0:47.5, unwrapped, fan on back, breathing deeply	0:50	37.45°
Unwrapped, fan on back, breathing deeply	1:04	37.48°
Unwrapped, fan on back, breathing deeply	1:08	37.42°
At 1:10.5, wrapped, breathing deeply	1:16	37.28°
Wrapped, breathing deeply	1:22	37.26°
Wrapped, breathing deeply	1:25	37.18°
Wrapped, breathing deeply	1:45	36.98°
Wrapped, breathing deeply	2:09	36.79°

Experiment 12. — S. M., subject. Mercury thermometer under tongue. Room temperature, 16.0° to 19.0° C.; time, 4:00 to 6:09 P.M.

Condition of Subject.	Time of Reading.	Blood Temp.
Wrapped, breathing quietly	0:00	37.70°
Wrapped, breathing quietly	0:10	37.82°
At 0:13, wrapped, breathes deeply	0:16	37.75°
Wrapped, breathing deeply	0:38	37.81°
Wrapped, breathing deeply	0:44	37.79°
At 0:47, unwrapped, breathing deeply	0:50	37.80°
Unwrapped, breathing deeply	1:04	37.79°
Unwrapped, breathing deeply	1:08	37.77°
At 1:09, wrapped, breathing deeply	1:18	37.53°
Wrapped, breathing deeply	1:23	37.47°
Wrapped, breathing deeply	1:27	37.57°
Wrapped, breathing deeply	1:45	37.30°
Wrapped, breathing deeply	2:09	37.20°

For a composite graph of these two experiments see Fig. IV.

Liebermeister[7] found essentially similar changes in axillary temperature with chilling of the skin.

The normal diurnal variation tends to bring the blood temperature to a maximum in the late afternoon or early evening[5], after which it slowly falls through the night. This fact probably accounts in part, although only in part, for the marked tendency to fall in the intervals betweeen chilling, exhibited in the three night experiments, 8 (Fig. IX.), 10 (Fig. III.) and 11, and in the latter parts of the two late afternoon experiments, 9 (Fig. V.) and 12, but much less evident in the early parts of 9 and 12.

However, for our purpose the significant fact is that blood temperature shows relatively little change throughout the experiments and that such changes as do occur in immediate response to cutaneous chilling are, thanks to the high efficiency

of the body's heat-regulating mechanisms, rather in the direction of a rise than of a fall.

Blood-pressure reactions to chilling: In the course of Experiments 11 and 12 above, blood-pressure estimations by the auscultatory method were made at five-minute intervals. Successive readings of systolic and diastolic pressure were, for Experiment 11: Subject wrapped, breathing quietly, 134-80. 134-80; subject wrapped, breathing deeply, 141-83, 138-80, 138-82, 138-78, 142-80, 138-80, 142-90; subject unwrapped, fan on back, breathing deeply, 138-90, 138-86, 132-83, 128-80; subject wrapped, breathing deeply, 132-80, 130-84, 130-84, 134-84, 134-80, 134-88, 136-86, 136-90, 134-90, 132-86, 134-90, 136-94. Readings for Experiment 12 were: Subject wrapped, breathing quietly, 148-90, 142-90, 140-90; subject wrapped, breathing deeply, 152-94, 144-92, 148-96, 146-92, 148-94, 148-94, 148-94; subject unwrapped, fan on back, breathing deeply, 150-94, 152-94, 155-94, 146-94; subject wrapped, breathing deeply, 152-100, 146-94, 144-94, 144-94, 148-94, 146-94, 144-96, 142-94, 144-96, 140-96, 146-94, 146-98.

Thus chilling the body surface caused no significant change in blood pressure — in one case apparently a few millimeters rise, in the other a few millimeters fall. Animal experiments have shown an initial rise, followed, in instances of extreme chilling with depression of blood temperature, by a progressive fall (3, page 125, and 6).

This auscultatory method is not above question. However, at least, these two experiments harmonize with data from many other sources in warranting the conclusion that the depression of superficial temperature with cutaneous chilling was not the result of lowered blood pressure.

Respiratory changes with chilling and their effects upon mucous-membrane temperature: Control experiments thus show that blood pressure and temperature changes do not contribute to the observed fall in mucous-membrane and skin temperatures with chilling. The skin-temperature depression may then be referred unqualifiedly to reflex vasoconstriction of the cutaneous vessels. However, one other factor had to be

considered as a possible contributor to the mucous-membrane temperature depression, i.e., changes in respiration with chilling; experiments showed, as a matter of fact, that such changes did play a part.

It was found that chilling caused an increase in the volume of respiratory exchange, and that such augmentation of respiration caused some depression in mucous-membrane temperature. For determining the first point, the subject was fitted with one pneumograph about his thorax and a second about his abdomen, both recording respiratory amplitude on a kymographion. Respiratory rate was counted by the observer and recorded on the drum. The observer wrapped and unwrapped the subject, who gave his attention to reading a novel.

Experiment 13. — S. M., subject. Reading novel. Abdominal and thoracic pneumographs. In the tables below the figure given in each case is the average for the last 15 respirations of each section of the experiment.

$$\text{"Product"} = \frac{\text{Abd. amplitude} + \text{Thor. amplitude}}{2} \times \text{Resp. rate.}$$

	Resp. Rate.	Abd. Amp.	Thor. Amp.	Product.
Subject wrapped	16	27.4 mm.	23.1 mm.	404
Unwrapped	20	25.3	19.8	451
Wrapped	16	25.7	23.7	395
Unwrapped, fan on back . .	20	25.6	22.2	478
Wrapped	17	28.6	23.7	445
Unwrapped, cold wet towels to back	20	27.5	21.3	488
Wrapped	16	31.7	26.2	463
Unwrapped, fan on back . .	20	34.5	28.1	626
Wrapped	16	28.5	22.1	405
Unwrapped, fan on back . .	20	33.7	27.5	612

It was further found that when respiratory rate was kept constant by breathing in time with a metronome, it was impossible for the subject to prevent his respirations from becoming deeper during chilling.

Experiment 14. — S. M., subject. Respiratory rate, 18 per minute. Pneumograph at level midway between xiphoid and umbilicus. Subject attempting to maintain respiration at depth of first part of experiment. Room temperature, 17.6° to 18.8° C.

Condition of Subject.	Time.	Ave. Resp. Amplitude.
Wrapped	0:00–0:01	16.6 mm.
At 0:02, unwrapped	0:13–0:14	25.2
At 0:16, wrapped	0:39–0:40	24.0
At 0:42, feet unwrapped; cold, wet towels around feet; fan on feet; at 0:52.5 legs and thighs unwrapped	0:58–0:59	32.8
At 1:00, back unwrapped; wet towel and fan on back	1:06–1:07	39.3
At 1:10, fan off, dried, wrapped	1:19–1:20	26

Ansiaux, also (6, page 569), upon immersing chloroformed dogs in cold water, found an increase in volume of respiratory exchange. Subsequently, after blood temperature had undergone a considerable fall, respiration decreased.

That increased volume of respiratory exchange could, under the conditions of our experiments, depress mucous-membrane temperature was shown by applying the mucous-membrane thermopile and comparing readings with quiet and forced respiration, other conditions remaining constant. With respiratory rate kept constant and the mean excursion of abdominal and thoracic pneumograph levels taken as an index of respiratory depth, it was found that an increase of depth amounting to seventy per cent caused an average maximum depression of mucous-membrane temperature of .71° C. developed in 19.25 minutes. These figures are the average for the first six crucial experiments to be described below.

The cause of this fall of mucous-membrane temperature with increased respiration may either be purely mechanical, i.e., due to direct cooling by the increased volume of cool air respired, or a local vasoconstrictor reflex in response to the cool air, or partly both. However that may be, the fact is of

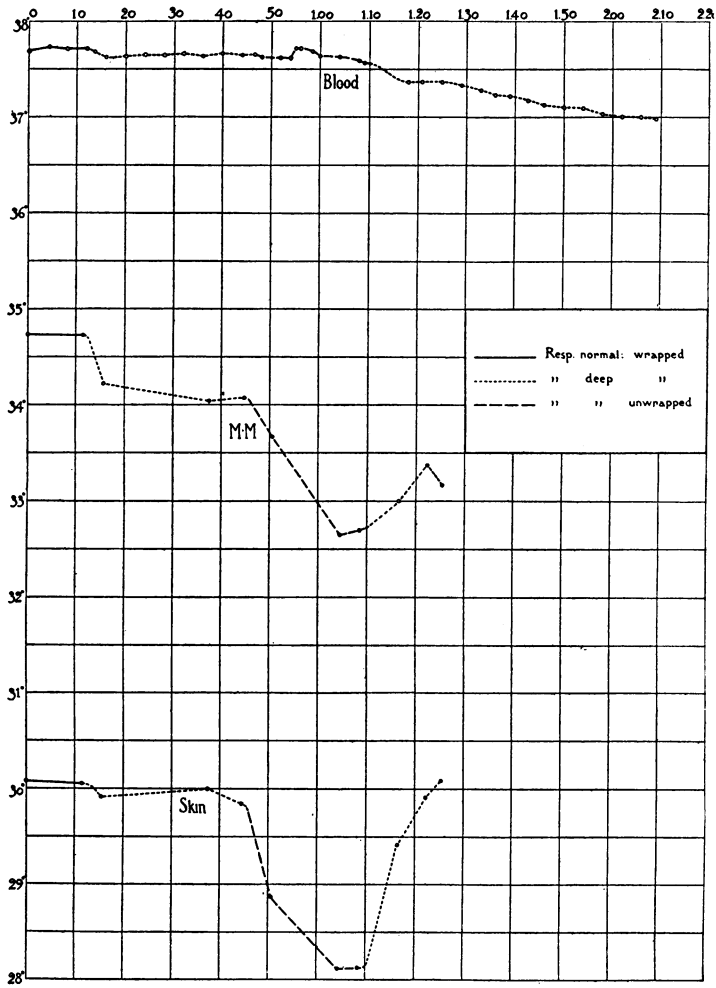

FIG. IV. — Effects of Chilling Body Surface, Respiration Controlled. Composite Graphs of Experiments 15, 16, 18 and 19 (Skin and Mucous-Membrane Temperatures) and Experiments 11 and 12 (Blood Temperature). Subject chilled by unwrapping, with draft of electric fan on back.

significance in showing that in any accurate thermogalvanometric study of mucous-membrane temperature changes, respiration must be carefully controlled. In all of our later experiments described below, respiratory rate was kept constant by breathing with a metronome, and depth registered by abdominal and thoracic pneumographs writing on a kymographion within sight of the subject. Galvanometer and thermometer readings were first taken during quiet respiration; the respiration was then increased in depth about seventy per cent, and, with the aid of isometric muscular contractions, maintained at this level throughout the rest of the experiment. Not until the mucous-membrane temperature, as indicated by galvanometer and thermometer readings, had reached a constant level with deep breathing, was the subject chilled.

IV. Normal vasomotor reactions to chilling of the body surface. — Changes in mucous-membrane and skin temperatures — amyl nitrite effects: The vasomotor responses of the exposed skin of the forehead and of the mucous membrane of the soft palate and oropharynx, with respiration and other conditions carefully controlled as described above, may readily be made out from Fig. IV. The two lower curves of this figure are composite graphs of four experiments of similar pattern (Nos. 15, 16, 18 and 19). The points chosen for plotting are: the first and last readings of each experiment, the readings immediately before and after each change in experimental conditions, and the first point of maximum response of the mucous membrane to changed conditions; each point graphed is the average value of the corresponding point of the four experiments. Time is plotted on the horizontal axis, temperature on the vertical; the space between the ruled lines represents ten minutes on the abscissa, one-half degree centigrade on the ordinate. The character of the lines connecting the points gives the nature of the experimental conditions, as indicated in the legend.

While respiration is quiet and the subject wrapped, mucous-membrane and skin temperatures remain constant. Deepening

of respiration affects only inconsiderably the skin temperature, but causes a depression of mucous-membrane temperature amounting to .68° C., which reaches its maximum after 25.4 minutes, and then, during the remaining 8.5 minutes before chilling begins, remains virtually constant.

The subject was chilled by unwrapping him and directing the draft of an electric fan against the lower thoracic region of his back. With the start of this process, a marked depression both of mucous-membrane and of skin temperature begins. The maximum fall of mucous-membrane temperature is 1.42° C., reached in 18.4 minutes. The synchronous point on the skin curve represents a drop of 1.73° C. The skin curve falls away a little more sharply than the mucous-membrane curve. However, even if the vasoconstriction in skin and mucous membrane were to follow an identical course, we should expect, on mechanical grounds, this difference in the curves; for the more exposed forehead would of course lose heat more readily than the mucosa of the palate and pharynx.

When it was seen the mucous-membrane temperature had ceased to fall, the fan was turned off and the subject again wrapped. Here a disparity in the behavior of skin and mucous-membrane vessels appears. The skin temperature climbs steeply and surmounts the level at which chilling began. The skin "reacts," as is commonly said. But the mucous-membrane temperature rises only .73° C. Its maximum recovery is reached after 12.7 minutes and is .69° C. below the last point before chilling. During the remaining 3.5 minutes of observation, it falls .21° C.

No merely physical reason is to be found for the mucous-membrane temperature remaining depressed; if its vessels returned to the same tone as before chilling, the temperature curve should return to control level. Yet this same incomplete recovery after chilling was noted in five out of six experiments, alike the early determinations with respiration uncontrolled and the final ones with respiration controlled. Measurement of the respiration records for the four experiments graphed in Fig. IV. was made, and the mean figure arrived at for respiratory amplitude before chilling differed from that after chilling

by only a fraction of one per cent. In those experiments in which respiration was slightly deeper before as well as in those in which it was a few per cent deeper after chilling, the failure of the mucous-membrane temperature to regain its former level is evident. (A single exception is Experiment 20, with the thermopile upon the faucial tonsil, in which control level was surmounted.) We are forced to conclude, therefore, that the vasoconstriction and ischemia reflexly produced in the palatine and pharyngeal mucous membrane by chilling the body surface persist in part for some time at least, and are not followed within a few minutes by a flush, as is typically the case with the skin.

The uppermost curve in Fig. IV. is a composite of two blood-temperature control experiments (11 and 12), which followed the same pattern as the two lower curves. For discussion, see Section III, above.

The several experiments may now briefly be discussed individually.

EXPERIMENT 15: S. B. G., subject. Mucous-membrane thermopile on posterior part of soft palate. Skin thermopile on forehead. Respiration, 12 per minute. Mouth open. Nose breathing. Thoracic and abdominal pneumographs. Room temperature 18° to 18.65° C.; time, 4:43 to 6:00 P.M.

Experiment 15 is given in full in tabular form. In the vertical column T is shown the time in hours and minutes from the start of the experiment; the other figures in the same horizontal row indicate the readings which correspond to the time in the first column. GS is the observed deflection in millimeters of the galvanometer when in circuit with the skin thermopile. S is the observed reading of the thermometer at the known-temperature end of the skin thermopile. TS is the computed temperature of the skin surface. TS = S + (GS x Calibration Constant) = S + .1004 GS. Similarly, GM = deflection of galvanometer in circuit with mucous-membrane thermopile. M = temperature at known-temperature end of mucous-membrane thermopile. TM = computed temperature of mucous-membrane surface = M + .1054 GM.

EXPERIMENT 15.

T.	GS.	S.	TS.	GM.	M.	TM.
Subject wrapped — breathing quietly.						
0 hrs. :00 min.	123 mm.	18.0° C.	30.35° C.	170 mm.	18° C.	35.92° C.
0:01	122.75	18.05°	30.37°	171	18°	36.02°
0:02	122	18.05°	30.30°	171.25	18°	36.05°
0:03	121	18.0°	30.15°	172.5	18°	36.18°
0:04	121.25	18.025°	30.20°	172	17° 19/20	36.08°
0:05	122	18.0°	30.25°	172	17° 19.5/20	36.10°
0:06	121.25	18.0°	30.17°	173	17° 19.5/20	36.21°
0:08.5 . . .	122.5	18.0°	30.30°	172	17° 19/20	36.08°
0:09.5 . . .	122.5	18.0°	30.30°	172	17° 19/20	36.08°
0:10.5 . . .	120.75	18.0°	30.12°	172.25	17° 19/20	36.11°
Subject increases depth of respiration.						
0:12.5 . . .	121	18.0°	30.15°	170	17° 19.5/20	35.90°
0:13.5 . . .	121	18.025°	30.17°	169.25	17° 19.5/20	35.83°
0:14.5 . . .	120.75	18.025°	30.15°	168.75	17° 19.5/20	35.78°
0:16	121	18.025°	30.17°	168.25	17° 19.5/20	35.73°
0:17	120	18.0°	30.05°	168	18°	35.72°
0:18	120	18.0°	30.05°	167	18°	35.62°
0:19.5 . . .	121	18.05°	30.20°	166.75	18°	35.59°
0:22	121	18.1°	30.25°	166.75	18° 3.5/20	35.76°
0:23.5 . . .	119.5	18.1°	30.10°	164.5	18° 3.5/20	35.52°
0:24.5 . . .	121	18.15°	30.30°	164	18° 3/20	35.44°
0:25.5 . . .	121.75	18.15°	30.37°	164	18° 3/20	35.44°
0:28.5 . . .	121	18.125°	30.27°	164	18° 3/20	35.44°
0:30	120	18.1°	30.15°	164	18° 2.5/20	35.42°

EXPERIMENT 15. — *Continued.*

T.	GS.	S.	TS.	GM.	M.	TM.
Subject unwrapped — fan on back.						
0:33	118	18.1°	29.95°	162	18° 3/20	35.24°
0:34	117	18.15°	29.90°	160.5	18° 4/20	35.13°
0:34.5 . . .	117	18.2°	29.95°	160	18° 4.5/20	35.10°
0:35.5 . . .	115.75	18.3°	29.92°	159	18° 5.5/20	35.05°
0:37	114.5	18.4°	29.90°	158.5	18° 7.5/20	35.09°
0:38.5 . . .	115.5	18.5°	30.10°	156.5	18° 9/20	34.96°
0:39.5 . . .	113.5	18.5°	29.90°	154.25	18° 9.5/20	34.75°
0:41	114	18.5°	29.95°	153	18° 10/20	34.64°
0:42	116	18.5°	30.15°	151.5	18° 10/20	34.47°
0:43	115	18.55°	30.10°	151	18° 11/20	34.47°
0:44.5 . . .	116	18.6°	30.25°	150	18° 11/20	34.36°
0:45.5 . . .	116.5	18.6°	30.30°	149	18° 11/20	34.25°
0:46.5 . . .	115	18.6°	30.15°	158	18° 11/20	35.20°
0:47.5 . . .	115.5	18.6°	30.20°	149.75	18° 11/20	34.32°
0:49.5 . . .	115.5	18.6°	30.20°	147	18° 11/20	34.04°
0:50.5 . . .	114	18.6°	30.05°	145.5	18° 11/20	33.89°
0:53.5 . . .	113	18.6°	29.95°	146	18° 12/20	33.99°
0:55	114	18.65°	30.10°	145.25	18° 12/20	33.91°
0:57	116.5	18.65°	30.35°	145	18° 12/20	33.88°
Fan off — subject wrapped.						
1:04	114.75	18.65°	30.17°	150.5	18° 13/20	34.51°
1:09	116	18.6°	30.25°	152.5	18° 12/20	34.67°
1:10.5 . . .	117	18.6°	30.35°	152	18° 11/20	34.57°
1:12	117.25	18.55°	30.32°	151	18° 10.5/20	34.44°
1:13.5 . . .	118	18.5°	30.35°	150.75	18° 10/20	34.39°

EXPERIMENT 15. — *Concluded.*

T.	GS.	S.	TS.	GM.	M.	TM.
Subject inhales ampoule of amyl nitrite.						
1:15.5 . . .	120	18.5°	30.55°			
Subject's face flushed.						
1:16.5 . . .	123	18.5°	30.85°			
1:17.5 . . .	118	18.5°	30.35°			

The mucous-membrane curve of Experiment 15 (Fig. V.) gives the typical picture of the composite graph described above. The skin curve is unique in the absence of definite depression of skin temperature with chilling. A later determination upon the forehead of the same subject showed the typical fall.

At the end of the experiment (1:14.5) the subject inhaled an ampoule of amyl nitrite. The alterations in superficial temperature were so swift that the attempt to follow both skin and mucous-membrane changes was unsuccessful. Observations were made, however, sufficient to show a steep rise of .5° C. in skin temperature, succeeded by an abrupt fall to normal.

These changes followed closely upon the observed transient flush of the subject's face and subsequent paling. Between the readings of 1:15.5 and 1:16.5, TS may well have risen higher than the point represented as the apex of the curve.

The uppermost curve of Figure V. is that of a blood-temperature control, Experiment 9.

EXPERIMENT 16: S. M., subject. M. M. thermopile on posterior wall of oropharynx. Skin thermopile on forehead. Respiration, 18 per minute. Nostrils plugged with cotton, mouth breathing. Thoracic and abdominal pneumographs. Room temperature, 19.0° to 20.6° C.; time, 10:11 P.M. to 12:33 A.M.

The curves of Experiment 16 (Fig. VI.) show the pharyngeal mucous-membrane reacting in essentially the manner indicated in the composite graph, and shown also for the palatine membrane in Experiment 15. The difficulties in technic are con-

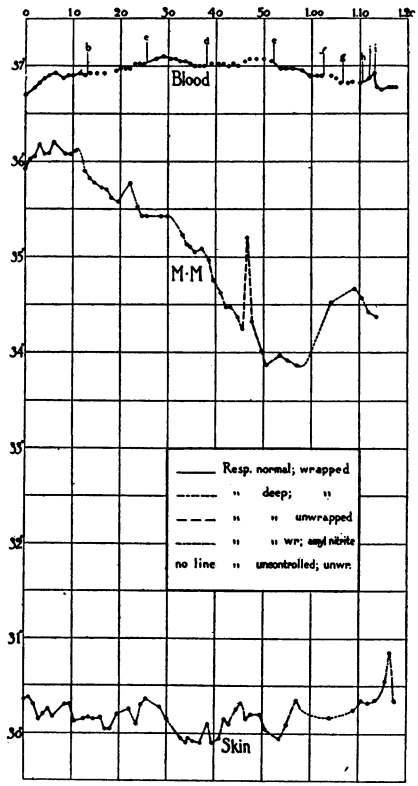

FIG. V. — Chilling and Amyl-Nitrite Effects. Experiment 15 (Temperatures of Skin and of Mucous Membrane of Soft Palate) and Experiment 9 (Blood Temperature). Experiment 9: *a*, wrapped; *b*, unwrapped; *c*, wrapped; *d*, unwrapped, fan on back; *e*, fan off, wrapped; *f*, unwrapped, iced towels applied to back; *g*, towels warm; wrung out in ice-water and reapplied; *h*, subject dried and wrapped; *i*, reading questionable.

siderably greater with the thermopile applied to the pharynx than to the palate, however, and the curve is never so smooth. The effects of moving the pharyngeal wall against the thermopile terminals by coughing, swallowing or clearing the throat,

is shown at 0:27, 0:50.5 and 1:41. Presumably two factors play a part in the sudden rise in temperature produced: the momentarily increased pressure between terminals and mucous membrane slightly increased, mechanically, the

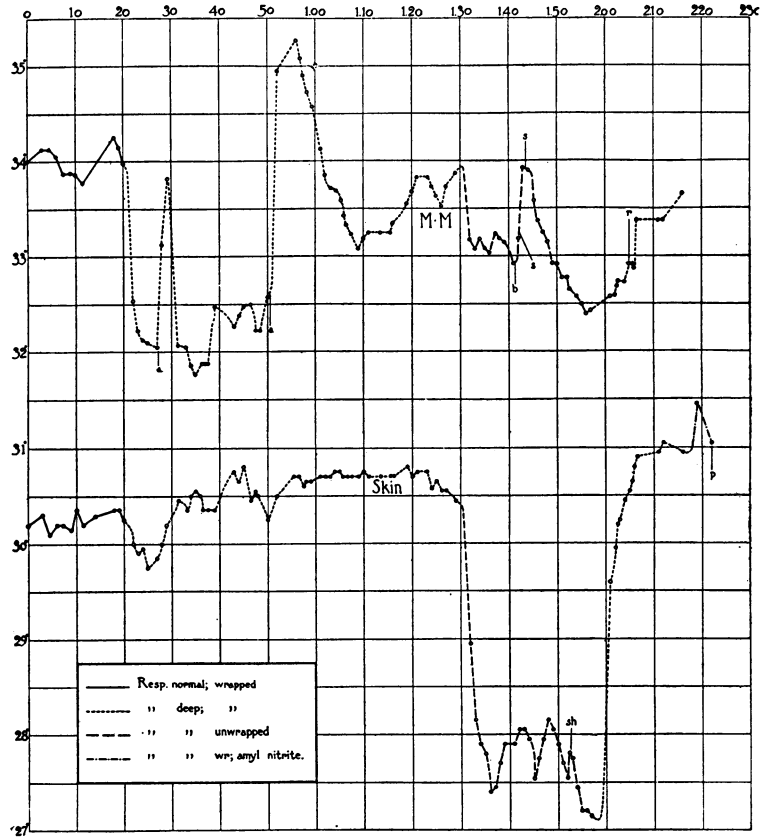

FIG. VI. — Effects of Chilling, Mechanical Irritation and Amyl Nitrite. Experiment 16 (Temperatures of Skin and Mucous Membrane of Oropharynx): *a*, coughs and clears throat; *b*, clears throat and swallows; *s*, swallows; *sh*, begins shivering; *r*, misses several respirations; *p*, exact time of point *p* not known.

temperature of the former; the painful mechanical irritation of the mucosa by the metal terminals and applicator probably caused a transient blush. The rises in temperature, which took place before chilling, although apparently elicited by less

movement, were much more marked than that which occurred during the active vasoconstriction with chilling — 1.77° and 2.69° as compared with .98° C.

The effect upon skin temperature of inhaling amyl nitrite is shown (2:17). A rise of .50° C. is again produced.

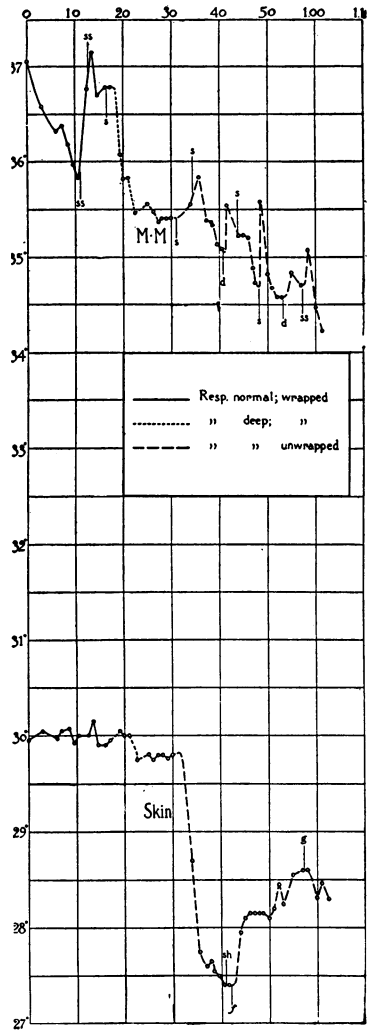

FIG. VII. — Effects of Chilling and Mechanical Irritation. Experiment 17 (Temperatures of Skin and Mucous Membrane of Oropharynx): *ss*, swallows twice, *s*, swallows; *d*, convulsive movement of pharynx; *sh*, begins shivering; *f*, fan slower; *g*, subject's shoes and socks removed.

It is to be remembered that, since the mucous membrane and skin curves of each experiment are synchronous, the annotations, although drawn in as though applying only to one curve, apply equally to both.

EXPERIMENT 17: S. M., subject. M. M. thermopile on posterior wall of oropharynx. Skin thermopile on forehead. Respiration, 18 per minute. Mouth closed; nose breathing. Thoracic and abdominal pneumographs. Room temperature, 19.1° to 20.1° C.; time, 4:24 to 5:27 P.M.

This experiment (Fig VII.) gives essentially the same picture as Experiment 16. It shows the behavior of the pharyngeal vessels to be the same with mouth closed and nose breathing as with nose plugged and mouth breathing. It again brings out the relatively slight and transient effect of mechanical irritation during chilling.

The experiment was unfortunately stopped by the subject's choking before he could be rewrapped.

EXPERIMENT 18: A. G. (Hebrew), subject. M. M. thermopile on posterior half of soft palate. Skin thermopile on forehead. Mouth open. Nose breathing (except where noted otherwise — see Fig. VIII.) Respiration, 18 per minute. Thoracic and abdominal pneumographs. Room temperature, 18.05° to 18.7° C.; time, 10:55 P.M. to 12:43 A.M.

This experiment tells the same story as the others. The picture is slightly atypical, however, because the subject was too sleepy to coöperate well. The early fluctuations in mucous-membrane temperature are due to changes in type of respiration (see legend, Fig. VIII.) The slow, steady fall of mucous-membrane and skin curves in the first half of the experiment is due to the subject being imperfectly wrapped.

The effect upon mucous-membrane temperatures of amyl-nitrite inhalation is well shown (1:42). A steep rise of 1.4° C. was followed by a somewhat slower fall. The rise is somewhat higher and less transient than that noted for the skin after amyl nitrite (*cf.* Figs. V. and VI.). However, this difference may well have been a mechanical effect due to the more exposed position of the skin, rather than the result of any greater degree of vasodilation in the mucous membrane.

EXPERIMENT 19: S. M., subject. M. M. thermopile on anterior half of soft palate. Skin thermopile on forehead. Respiration, 18 per minute. Mouth open, nose breathing. Thoracic and abdominal pneumographs. Room temperature, 17.9° to 18.8° C.; time, 3:55 to 5:16 P.M.

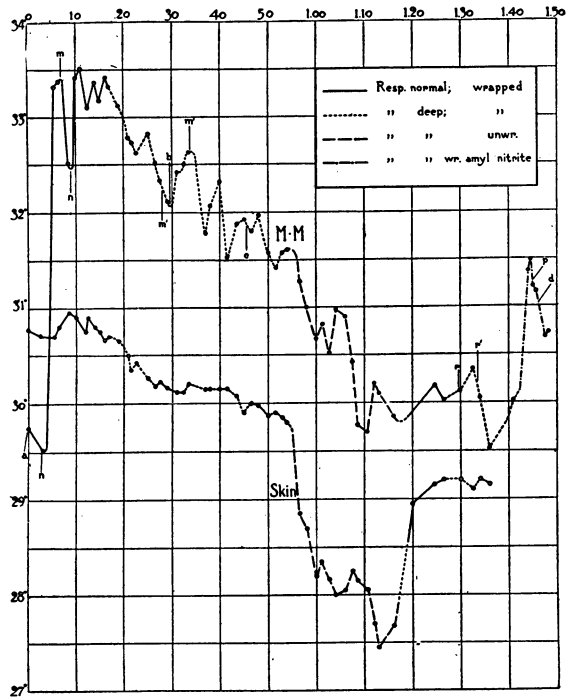

FIG. VIII. — Chilling and Amyl-Nitrite Effects. Experiment 18 (Temperatures of Skin and Mucous Membrane of Soft Palate): *a*, breathing through mouth; *n*, changes to nose breathing; *m*, changes to mouth breathing; m^1, breathes through mouth momentarily; *b*, touches mucous-membrane applicator; *c*, abdomen seen to be uncovered (this had been true for some time); *p*, looks pale; *d*, feels cold; *r* to r^1, respiration a little deeper than deep control.

Experiment 19, from 0:00 to 0:50, shows the typical picture save that the anterior palatine mucous membrane is not affected by deepening respiration. At 0:50 the subject's feet were exposed, wrapped in cold, wet towels and the electric fan turned on them. This seems to have been without effect upon

the forehead, but was followed, apparently, by a slight depression, .29° C., of mucous-membrane temperature. This

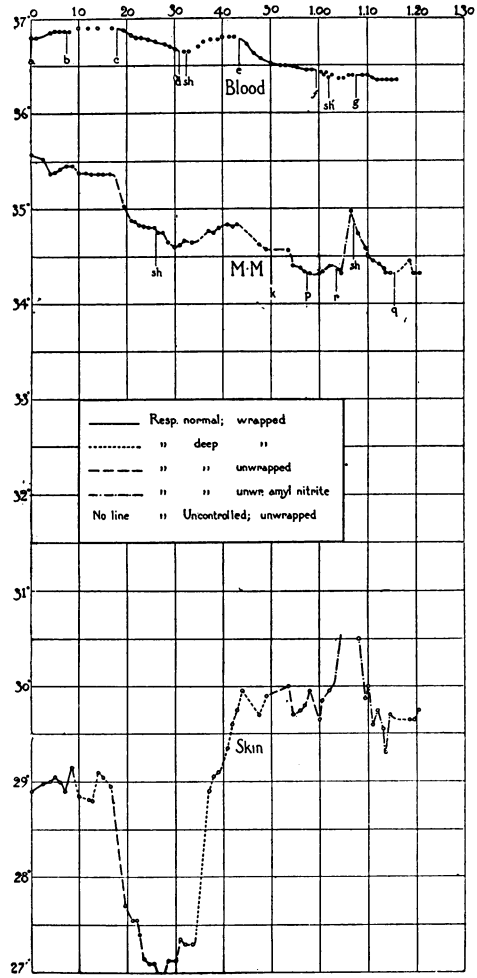

FIG. IX. — Chilling and Amyl-Nitrite Effects. Experiment 19 (Temperatures of Skin and Mucous Membrane of Soft Palate) and Experiment 8 (Blood Temperature): *a*, wrapped; *b*, unwrapped; *c*, wrapped; *d*, unwrapped, fan on back; *sh*, shivering begins; *e*, fan off, wrapped; shivering stops; *f*, unwrapped, cold wet towel to back; sh^1, is shivering; *g*, dried and wrapped; *k*, cold wet towels to feet, fan on feet; *p*, more cold water poured on towels around feet; *r*, respiration is exaggerated; *q*, fan off, feet dried and wrapped.

effect was not sufficiently definite to warrant much emphasis, but is at least suggestive in view of the possible efficacy of wet feet in exciting colds.

Administration of amyl nitrite at 1:03, while the feet were still being chilled, was followed by the typical rise in mucous-membrane and skin temperatures. The break in the skin-temperature curve is meant to indicate that it may have

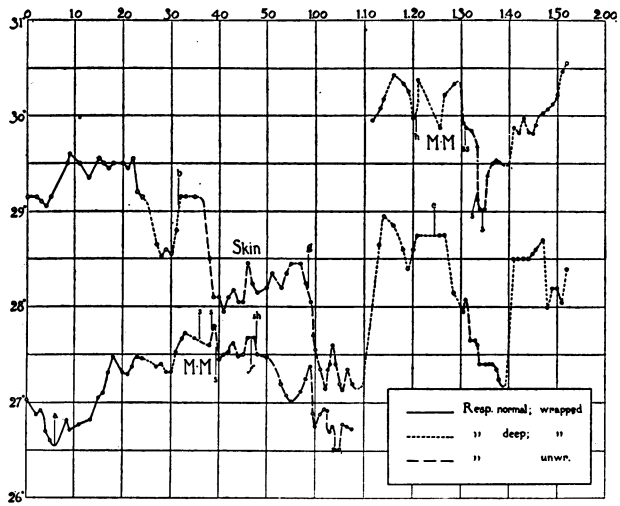

FIG. X. — Chilling Effect. Experiment 20 (Temperatures of Skin and Mucous Membrane of Faucial Tonsil): *a*, slight readjustment of mucous-membrane applicator; *b*, subject feels warmer; *s*, swallows; *f*, fan faster, shoes and socks removed; *sh*, begins shivering; *g*, fan faster; *h*, dorsum of subject's tongue momentarily against applicator; *c*, feels cold; *ss*, swallows twice.

risen above 30.50° C. in the interval, 1:02 to 1:08, during which no skin readings were made.

The uppermost curve in Fig. IX. is a blood-temperature control, Experiment 8.

EXPERIMENT 20: S. M., subject. M. M. thermopile on left faucial tonsil, upper half, skin thermopile on forehead. Nostrils plugged; mouth breathing. Respiration, 18 per minute. Thoracic and abdominal pneumographs. Room temperature, 17.5° to 18.7° C.; time, 1:06 to 2:58 P.M.

The mucous-membrane curve (Fig. X.) shows with chilling a characteristic depression. How to account for the abrupt upward shift at the time the subject was wrapped, 1:08, we do not know; however, we believe that it was an artefact, and did not accurately represent a vasomotor change. The subject was chilled a second time, 1:29.5 to 1:39; the curve again showed the usual fall. Recovery after chilling was atypical over the tonsil, in that temperature rose above control level.

The mean values for the changes shown by these six experiments may be summarized as follows:

Maximum fall with deepened respiration for TM = .71° C. in 19.25 minutes. Synchronous fall for TS = .15° C.

Subsequent change before chilling for TM = .085° C. rise in 6.5 minutes. Synchronous change for TS = .017° C. fall.

Maximum additional fall with chilling for TM = 1.33° C. in 19.4 minutes. Synchronous fall for TS = 1.54° C.

Subsequent change before wrapping for TM = .13° C. rise in 3.4 minutes. Synchronous change for TS = .05° C. fall.

Maximum rise after wrapping for TM = .75° C. in 12.8 minutes. Synchronous rise for TS = 1.67° C.

Subsequent change for TM = .17° C. fall in 2.8 minutes. Synchronous change for TS = .15° C. rise.

The behavior of the mucous membrane of the nasopharynx was studied by means essentially similar to the foregoing. However, the other mucous surfaces were investigated in July and August, 1918; the nasopharyngeal experiment was performed in January, 1919, and with a succession of conditions slightly different from those of the earlier determinations. Vasoconstriction with chilling and a partial recovery on wrapping were even more strikingly shown in the nasopharynx than in the membranes previously studied.

An applicator (Fig I., E) of somewhat smaller galvanized iron wire (No. 13) was slung as before by an adhesive strip under the superior incisor teeth. The long arm of the applicator, arching slightly so as to clear the dorsum of the tongue, extended backward to the posterior margin of the soft palate; at this point it was bent forward through about 110 degrees

to form the short arm, which extended upward in a slight curve whose convexity was anterior. To the tip of the short arm the thermopile terminals were attached, and were held by it against the posterior wall of the nasopharynx about one centimeter to one side of the mid-line and about 2.5 to 3 cm. above the posterior border of the soft palate.

EXPERIMENT 21: S. M., subject. M. M. thermopile on posterior wall of nasopharynx. Skin applicator on forehead. At first, nostrils plugged, breathing through mouth; later, breathing through nose, mouth open. Respiration, 18 per minute. Thoracic and abdominal pneumographs. Room temperature, 15.7° to 16.9° C.; time, 4:15 to 5:45 P.M.

With the anterior nares plugged and the soft palate raised in mouth breathing, the nasal chamber was virtually a closed cavity, whose temperature did not vary with the rate of blood flow through its walls. Correspondingly, the mucous-membrane curve (Fig. XI.) showed no certain change when, at 0:08.5, respiration was deepened, nor at 0:22, when the subject was unwrapped and chilled with the electric fan. The skin curve, on the other hand, dropped off characteristically, to recover when the subject was rewrapped.

At 0:46 the nostrils were unplugged and nose-breathing began. The nasopharynx at once came into free communication with the outer air, was cooled by each respiration, and became dependent upon its blood supply for maintenance of its temperature. When equilibrium had been reached, the subject was again, at 1:07.5, unwrapped and chilled with the fan. Mucous-membrane and skin temperatures fell together, the former reaching a maximum depression of 1.83° C. in six minutes, the latter of 1.95° in eight minutes. After rewrapping at 1:16, the mucous-membrane temperature rose in six minutes to a maximum point .38° below the control level, then fell slightly; the skin temperature mounted in four minutes to a maximum only .10° below control level.

Checking of quantitative results by qualitative observations of redness: The experimental analysis described above adequately proves, it seems to us, that chilling of the body surface reflexly produces vasoconstriction in the vessels supplying

the normal mucous membranes of the palate, tonsils, oropharynx and nasopharynx. However, in order to secure still further corroboration, observations of the appearance of the mucous membranes and their blood vessels were made.

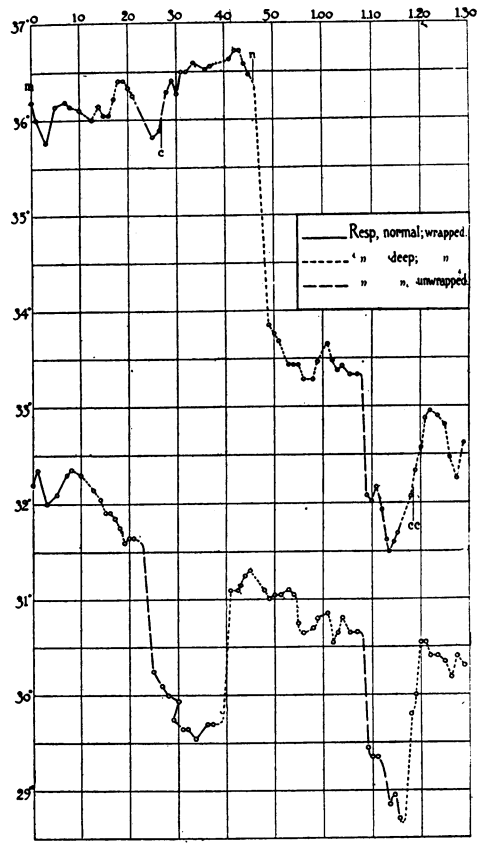

FIG. XI. — Chilling Effect. Experiment 21 (Temperatures of Skin and Mucous Membranes of Nasopharynx): *m*, nostrils plugged, breathing through mouth; *c*, coughs; *n*, plugs removed from nostrils; breathes through nose; *cc*, coughs three times.

Twelve experiments were performed. Of the five observers who noted the appearance of the buccal and oropharyngeal membranes before and after direct exposure of those membranes to cold air, all were of the opinion that, with the direct

chilling, blanching occurred. Of the six observers who noted the appearance of the soft palate and the seven who studied the normal oropharynx before and after chilling of the body surface, all said that the membranes paled while the skin was being chilled. Only one observer specifically studied the reaction of the tonsils. He said that they blanched during the skin's chilling. Of the three observers who watched the changes following rewrapping, one simply said that reddening occurred; two said that reddening occurred only to a slight extent.

The first point, i.e., the response of the mucous membranes to direct chilling, was not suitable to thermogalvanometric study. The other points observed are wholly in accord with the quantitative studies.

V. Vasomotor reactions of abnormal tissues. — Reactions in chronic inflammatory throats: One new point of great interest was brought out by the observation experiments in which the pillars and tonsils were seen to blanch with the cutaneous chilling. The pharynx of this same subject was much injected. He gave a history of having noticed a sore throat about a week before, which he thought had cleared up; the night before the experiment he had driven an open machine without an overcoat, and his sore throat had returned. The diagnosis was chronic catarrhal pharyngitis with pustules. This inflamed throat did not pale with the rest of the mucous membrane, but, if anything, its injection was intensified by chilling the body surface.

In a thermogalvanometric experiment upon a case of chronic pharyngitis of two years' standing, a similar reaction resulted (Fig. XII.).

History. — J. D. R. Began smoking 1915; used about four cigarettes daily. In 1916, began smoking fifteen to twenty cigarettes daily; about this time pharyngitis began. Since has smoked eight to ten daily. Treated April, May and June, 1917, Johns Hopkins dispensary, with argyrol, etc. No improvement. Treated twice a week with argyrol and silver nitrate, November and December, 1918, in Washington University dispensary. No improvement. Told smoking was probable cause, and if would stop smoking throat would get well. Condition unchanged August 2, 1918, when experiment was performed.

EXPERIMENT 22: J. D. R., subject. M. M. thermopile on inflamed posterior wall of oropharynx. Skin thermopile on forehead. Respiration, 13 per minute. Nostrils plugged; mouth breathing. Thoracic and abdominal pneumographs. Room temperature, 18.7° to 19.5° C.; time, 10:10 to 11:35 P.M.

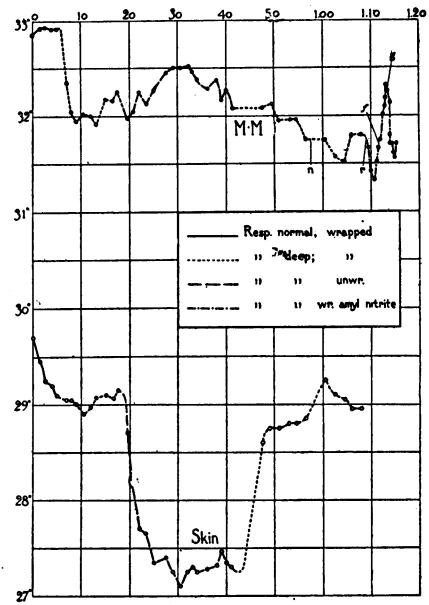

FIG. XII. — Chilling and Amyl-Nitrite Effects upon Chronically Inflamed Oropharynx. Experiment 22 (Temperatures of Skin and Mucous Membrane of Oropharynx): *n*, plugs pulled from subject's nose; begins nose breathing; *r*, respiration suddenly deepened; *f*, face flushed, *g*, flush passing; respiration still exaggerated.

The skin curve in Fig. XII. is typical. The mucous-membrane temperature shows the fall with deepened respiration which of necessity would follow inhalation into the pharynx through the open mouth of increased volume of cold air. However, with chilling, 0:18.5 to 0:42, the mucous-membrane temperature, instead of dropping with the skin temperature, shows a slight transient rise. The shape of the curve, reaching its height in the middle of the period of chilling and then slowly sinking, apparently uninfluenced by the cessation of chilling,

suggests that it records some slight changes in local vasomotor tone quite independent of the cutaneous chilling, or alterations in general blood pressure, or some slight accidental change in experimental conditions. At all events there is no questioning the fact that the normal reflex vasoconstriction is absent.

Inhalation of an ampoule of amyl nitrite (1:08 to 1:09.5) was followed by characteristic vasodilation. Measurement of the respiration record shows breathing to have been suddenly deepened at 1:09 (Fig. XII., r) and to have maintained itself

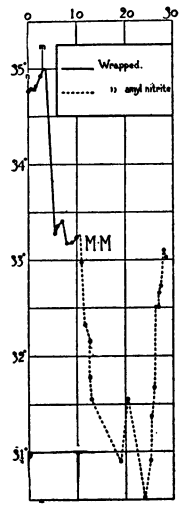

FIG. XIII. — Effect of Amyl Nitrite upon Acutely Inflamed Soft Palate. Experiment 23 (Temperature of Mucous Membrane of Soft Palate): *n*, breathing through nose; *m*, changes to mouth breathing.

abnormally deep until 1:14.5, when the subject could no longer maintain the slow rhythm, and respiration became quick and shallow. The preliminary fall of mucous-membrane temperature from 1:09 to 1:10.5 was doubtless due, therefore, to deepened respiration and a fall in general blood pressure; the rise from 1:10.5 to 1:13.25 was unquestionably due to local vasodilation and occurred in spite of deepened respiration and lowered blood pressure.

Amyl nitrite causes vasodilation by direct action upon the smooth muscle of the blood-vessel walls.[8] This typical dilator

response of the inflamed throat to amyl nitrite shows, therefore, that the vessel walls are capable of reacting normally. The typical skin curve would indicate proper functioning on the part of the afferent and association elements of the reflex arc. This failure of normal reaction to cutaneous chilling, in so far as conclusions can be drawn from a single experiment, must then be referred to the motor elements of the reflex arc, and probably has its seat in or near the inflamed mucous membrane.

Reaction to amyl nitrite of an acute inflammatory palate:

EXPERIMENT 23: S. B. G., subject. M. M. thermopile upon the intensely injected soft palate. Acute pharyngitis and tonsillitis. Respiration uncontrolled. Mouth breathing (except 0:00 to 0:03).

At 0:10.5 (Fig. XIII.) subject inhaled by mouth an ampoule of amyl nitrite. A steep fall of mucous-membrane temperature, amounting to 2.69° C., followed. The minimum temperature was reached in 13.5 minutes, and was followed by a rise of 2.56° C., attained in four minutes.

Evidently the vessels of the inflamed membrane were practically maximally dilated. The temperature change observed was therefore the result of the increase in depth of respiration and the depression of general blood pressure.

Reflex reactions of scar tissue to chilling:

EXPERIMENT 24: A. S. (Hebrew), subject. Keloid removed from chest wall August 24, 1918. Experiment performed September 25, 1918. Scar at that time 2.5 by 1 cm.; red; covered with epithelium. First thermopile on normal skin of chest near scar. Second thermopile on scar. Room temperature, 21.35 to 21.6° C. (See Fig. XIV., curves on left.)

The subject sat wrapped from 0:00 to 0:11.5; the sites of application of the thermopiles were of course freely exposed. At 0:11.5, the subject was bared from the waist up, and chilled with ice bags to her back. Skin and scar temperatures both fell sharply. The scar temperature reached a maximum depression of .90° C. in 1.0 minute, the skin of 1.12° C. in 4.5

minutes. At 0:17.5, the subject gasped and heaved her chest. Possibly as a result of mechanical irritation, the scar temperature at once rose, although skin temperature was not affected. At 0:20.75 the subject stood up to wrap herself, and may have disturbed the position of the scar applicator, although no dis-

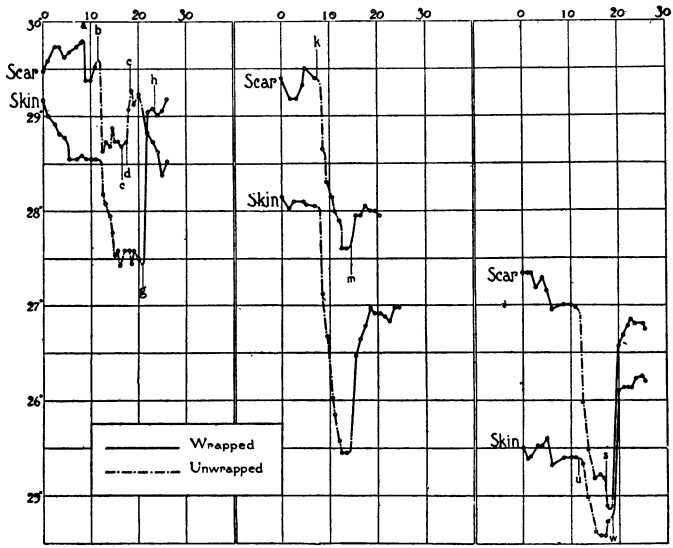

FIG. XIV. — Reflex Effects of Chilling on Scar Tissue. Experiments 24, 25 and 26 (Temperatures of Scars and Contiguous Skin). Experiment 24: *a*, subject moves, sighs, etc.; *b*, subject bared from waist up; ice bags to back; *c*, gasps; *d*, gasps, heaves chest; *g*, wrapped (subject stood up to wrap self; when she sat down again the skin applicator was found to have tilted; the scar applicator seemed all right, but it also had probably moved somewhat); *h*, heaves sigh. Experiment 25: *k*, body bared from waist up; no fan or icebag used; *m*, wrapped. Experiment 26: *u*, body bared from waist up; fan on back; hairs on forehead not disturbed at all by draft; *s*, shivers; *w*, fan off, wrapped.

placement was visible. After wrapping, the skin temperature rose typically, the scar temperature fell.

This experiment on new scar tissue shows, certainly, reflex vasoconstriction in response to chilling. To what degree the later atypical behavior of the scar temperature actually represents its vasomotor reactions and to what the failure of the subject to coöperate, it is difficult to say.

EXPERIMENT 25: E. E., subject. Radical operation June 7, 1918, for carcinoma of breast. Experiment performed September 23, 1918. First thermopile on normal skin near scar. Second thermopile on red scar, covered with epithelium, circular, about 2 cm. in diameter, over site of amputated breast. Sites of application exposed throughout experiment (see Fig. XIV., middle curves). The subject was chilled at 0:07.5 merely by unwrapping in the cold room. Scar temperature dropped 1.80° C., within 5.0 minutes; skin temperature, 2.63° C. within 5.0 minutes. Upon rewrapping at 0:14.5, scar temperature rose .45° C. in 3.0 minutes; skin temperature, 1.54° C. in 4.0 minutes.

EXPERIMENT 26: L. S., subject. Admitted St. Louis Children's Hospital, February 1, 1918, with history of having had ulcer on forehead for a year. Diagnosis: syphilitic ulcer. Slow improvement under specific treatment. June 21, 1918, skin graft to ulcer from leg. Favorable. Discharged July 7, 1918. Experiment performed September 12, 1918. Scar about 5 cm. in diameter, red, covered with thin epithelium. First thermopile on normal skin near scar. Second thermopile on scar. Room temperature, 17.8° to 17.95° C.

At 0:11.5 the subject was bared from the waist up, and an electric fan turned on her back. Hairs over her forehead were not disturbed; thus the sites of application were not cooled by draft. The scar temperature fell 2.09° C. in 6.0 minutes, the skin 0.82° in 4.5 minutes. Upon wrapping at 0:18.5, scar temperature rose 1.96° C. in 4.0 minutes; skin, 1.55° C. in 6.5 minutes.

These reactions would seem to explain the cyanosis of fresh scars during cutaneous chilling. The arteriolar constriction doubtless renders the flow of blood through the wide capillary network scant and sluggish, thus allowing unusually complete absorption of oxygen from the oxyhemoglobin.

VI. After-effects of chilling. — *S. B. G.*, after being chilled as subject for fourteen experiments over a period of twenty-two days in midsummer, developed severe rhinitis, followed quickly by pharyngitis, tonsillitis and injection of uvula and soft palate. Subject retained an abnormal susceptibility to colds throughout fall and early winter.

S. M., after being chilled as subject for fifteen experiments over a period of twenty-four days in midsummer developed a slight neuralgia in left shoulder. Next day was again subject. The day thereafter pleurisy developed in left chest. Neuralgia yielded to local treatment. Pleuritic symptoms lasted two weeks. Mucous membranes remained normal.

Chilled again in November without ill-effect. Chilled December 4; experiment 4:00 to 6:00 P.M. By following morning slight congestion in nasopharynx had developed, which persisted three or four days. Chilled January 2 without after-effect other than nausea, vomiting and headache.

This subject noticed that entering the cold room from the hot outside air of summer was frequently followed by violent intestinal peristalsis and defecation. This subject irrigated his nose and throat after each exposure with a weakly alkaline salt solution, used *hot*, with the idea both of cleansing and of producing hyperemia. A spray of .5 per cent phenol in liquid albolene was used after the winter exposures.

A. G. On August 1, chilled (see Experiment 18). After exposure, low-grade pharyngitis developed and persisted some days.

J. D. R. Subject thought after Experiment 22 there was exacerbation of pharyngitis.

G. A. Suffered no ill-effects from Experiment 6 other than headache.

B. J. F. No symptoms after an observation experiment.

VII. Discussion. — Simple acute infections of the nose and throat may be considered, for convenience of discussion, as falling roughly into two groups:

First, those in the etiology of which the event of prime importance is the arrival upon the mucous membranes of the virus. Such infections tend to occur in epidemic form, for example, epidemics of streptococcus pharyngitis. Certain coryzas fall into this group according to recent studies by Kruse[9] and by Foster[10], with a filterable virus as the causative agent.

In the second group, with which this paper is primarily concerned, the virus is already present as a part of the harmless flora of the upper respiratory tract, and becomes an active infective agent only through a change in its relationship to the host. The explanation commonly assigned for this altered relationship is increased virulence of the organism or decreased resistance of the host. Since host is more complex than parasite and more susceptible to change with altered environment, lowered resistance would seem the more frequent and probable cause.

Experimental inquiry as to how exposure to cold can alter the relation of host to parasite in such a way as to give rise to infection seems to have been made almost entirely upon animals. The literature to 1908 is reviewed by Marchand (3, page 133). That animals whose blood temperature has been lowered may show decreased resistance to bacterial infection has been proven by many authors. Trommsdorf [11] further showed in such animals a decreased motility and phagocytic activity of the leucocytes and a diminished capacity for regeneration of alexine and for elaboration of specific antibodies. But, as Marchand himself says, and as our experiments would indicate (see Section III. above), no such considerable lowering of body temperature occurs in the great majority of instances of exposure responsible for excitation of the common upper respiratory infections. Conditions in the existing animal experiments are not properly comparable to the conditions of "catching cold" in man; we must look elsewhere for an explanation.

The theory commonly advanced is that cutaneous chilling, driving the blood inward, produces, by mechanical or reflex means, or both, congestion of the internal organs. Indeed such congestion has been demonstrated in animal experiments by a number of authors: Lassar[12] sectioned the lungs, livers and hearts of animals after immersion in ice water, and found their vessels greatly dilated. Schüller[13] has shown congestion of the arteries and veins of the pia mater in animals chilled by application of cold compresses. Rossbach[14], Kisskalt[15] and others have made similar observations upon the epithelium of the exposed trachea. Winternitz[16] has demonstrated an increase in the volume of the arm of a human subject immersed in a cold sitz-bath, a decrease in the arm's volume when the bath water was warm.

Many authors have assumed that such findings apply equally well to the human nose and throat. The common observation that chilling of the body surface may in a few minutes be followed by a feeling of congestion in the nose, presumably due to an increased amount of blood in the erectile turbinate bodies, has seemed to lend plausibility to such an

assumption. That it is nevertheless absolutely at variance with what actually occurs in the nasopharynx, oropharynx, tonsils and palate is shown by the present experiments. The behavior of the specialized turbinate bodies we have not determined.

As to the effect of the demonstrated ischemia of the buccal and pharyngeal mucous membranes upon their resistance to the pathogenic bacteria present, we are confined largely to inference and reasoning *a priori*. Direct experimental investigation of the matter has unfortunately been delayed by the wrong assumption that congestion occurred.

Jonathan Wright, in a scholarly consideration of the etiology of acute inflammations of the nose and throat[1] says:

> " It may well be, as has been admitted, that certain bacteria are at once pathogenic when they reach the mucous membrane. Indeed, this seems very probable when they reach the mucous membranes of certain individuals. It may well be that such individuals always present, owing to systemic states, conditions of the mucosa which offer an ever-open avenue to infection; but granting all this, which indeed is in reality a part of our conception of the mechanism of the process, it seems extremely likely that local biochemical change, dependent upon molecular activities acting through the sympathetic nervous system, is the antecedent in the majority of cases of bacterial infection. This molecular disturbance of the normal activities of the sympathetic nerves may be set up by external or internal agencies, by the chilling of the body surfaces, or by derangements in the activities of the internal organs. Owing to the fact that wet feet and the chilling of distant regions of the surface of the body are, at least in clinical experience, quite as frequently followed by coryzas and sore throats as the direct impact of such external influences upon the head and neck, we have the right to infer that the shock at the surface must be transferred to internal nerve ganglia and there translated into impulses which are carried to the surfaces of the mucosa of the upper air passages. There they give rise to the chain of biophysical and biochemical changes which may simply result in a mild coryza or a catarrhal pharyngitis, the resolution of which terminates the chain, or these conditions may be in themselves the starting point of bacterial invasion."

In the insufficient light of present knowledge, it would seem not improbable that the ischemia incident on cutaneous chilling, by decreasing cell respiration, or by retarding removal of the products of cell metabolism, or by increasing the permeability of the epithelial cell surfaces to the bacterial products,

or by decreasing the local supply of specific antibodies, or by altering the media in the tonsillar crypts and folds of the pharyngeal mucosa in which the bacteria are living, or by a combination of these factors, might effect the local change postulated by Wright and thus so disturb the equilibrium between host and parasite as to excite infection. We here use the term "infection" as denoting a process separable from that of invasion or penetration of the bacteria into or through the mucosa. For study of tonsils in the early stages of infection has usually shown the crypts swarming with bacteria with none demonstrable beneath the mucosa surface (1, page 291), [17], [18]. There is much collateral evidence to support the hypothesis of Wright that a factor other than any of those suggested above — namely, the surface-tension relations of bacteria and mucosa cell surfaces [19] — enters into the determination of penetration or non-penetration of bacteria through the mucosæ. This hypothesis certainly deserves experimental investigation.

The demonstration that cutaneous chilling causes reflex vasoconstriction and ischemia in the nasopharynx, oropharynx, tonsils and palate at least furnishes a new and correct point of departure for future investigation, to replace the former false assumption of congestion.

VIII. Summary. — 1. A method and instruments are described by means of which changes in the temperature of the skin and exposed mucous surfaces of human subjects may be followed quantitatively. The method consists essentially in holding in opposition with the surfaces, by means of specially devised "applicators," the terminals of a thermopile in circuit with a D'Arsonval galvanometer. From the thermometer and galvanometer readings the absolute temperature at any time of the surface beneath the thermopile junctions is readily computable.

2. By this thermogalvanometric method the temperature of the skin and oral and pharyngeal mucous membranes was shown to fall with chilling of distant areas of the body surface and to rise again on rewrapping the subject.

3. Control experiments showed the blood temperature relatively unaltered by such cutaneous chilling; such small changes as were effected were in the direction of a minute rise with chilling and a fall on rewrapping.

4. Two control experiments showed no consequential changes in blood pressure with cutaneous chillings. Animal experiments have resulted in a rise of blood pressure with chilling.

5. An increase in volume of respiratory exchange was found to result from cutaneous chilling. Such respiratory increase usually caused a depression of mucous-membrane temperature. In studying mucous membranes by this method it is therefore necessary that respiration be carefully controlled. In all the crucial experiments whose individual graphs are published above, the respiration was kept constant by a metronome, a thoracic and an abdominal pneumograph.

6. Changes in temperature of the skin or exposed mucous surfaces, under the conditions of our experiments, are thus shown to be the result of changes in vasomotor tone in the vessels supplying those surfaces. A fall in superficial temperature indicates vasoconstriction; a rise, vasodilation.

7. Chilling of the body surface causes reflex vasoconstriction in the skin of the head and neck. Recovery after cessation of chilling is typically quick and complete; often the superficial temperature rises above the control level, i.e., that before chilling. Inhalation of amyl nitrite causes a sharp rise of the skin curve, corresponding to the flush of the face, followed by a steep fall.

8. Earlier attempts at explaining the excitation of pharyngeal and tonsillar infections by cutaneous chilling have been based upon the assumption that such chilling causes congestion of the mucous membranes. These experiments show, on the contrary, that *chilling of the body surface causes reflex vasoconstriction and ischemia in the mucous membranes of the palate, faucial tonsils, oropharynx and nasopharynx.* The quantitative temperature determinations showing this point were corroborated by qualitative observations of color change.

Recovery after cessation of chilling is incomplete. Typically the mucous-membrane curve reached within six to twenty minutes after cessation of chilling a maximum on the average .55° C. below control level, and, during the few minutes thereafter that the experiments were continued, fell slightly. The tonsillar curve of recovery was exceptional in that it rose above control level. Inhalation of amyl nitrite, either during or after chilling, was followed by a steep rise and fall in the mucous-membrane curves quite similar to those of the skin. Mechanical irritation is apparently also capable of checking momentarily the vasoconstriction during chilling and of causing a slight transient vasodilation.

9. The oropharyngeal curve of a case of chronic pharyngitis of almost two years' standing showed no depression with chilling. Normal vasodilation followed inhalation of amyl nitrite. The reflex arc to the mucous-membrane vessels had thus presumably been interrupted in its peripheral motor elements by the chronic inflammatory process, or by the factors producing the inflammation. A throat, with a history of inflammation extending back only a week, similarly showed on inspection no blanching with chilling.

10. The curve of an acutely inflamed soft palate was markedly depressed by inhalation of amyl nitrite. Evidently the vessels were virtually maximally dilated in the inflammation, and the fall in temperature was due to lowered blood pressure and increased respiration.

11. Scar tissue showed reflex vasoconstriction parallel to that of the neighboring skin. The earliest scar tested and thus proved to have vasomotor fibers was at the site of an operation, performed a month before, for removal of a keloid.

12. In four instances, exposure was followed by a "cold" or sore throat. The mucous membranes of one subject remained normal after sixteen exposures.

13. It does not seem improbable that the ischemia of the mucous membranes resulting from cutaneous chilling might so disturb the equilibrium between the host and the bacteria in the tonsillar crypts and folds of the pharyngeal mucosa as to excite infection.

The disinterested and expert observation needed in the study of mucous membrane color changes was accorded us by Dr. G. E. Hourn, Dr. A. F. Koetter, Dr. C. A. Gundelach and Dr. F. L. Morgan, laryngologists, and by Dr. M. T. Burrows and Dr. L. C. Bean of the Department of Pathology, whom we would take this occasion to thank.

It is a pleasure to thank the many members of the Faculty of Washington University Medical School for facilities extended us, and our friends who have acted as subjects; also Dr. C. K. Drinker of Harvard for the courtesies of his laboratory, and Professor Lindley Pyle, Dr. Jonathan Wright and Professor W. J. V. Osterhout for advice upon many points.]

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